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rubella

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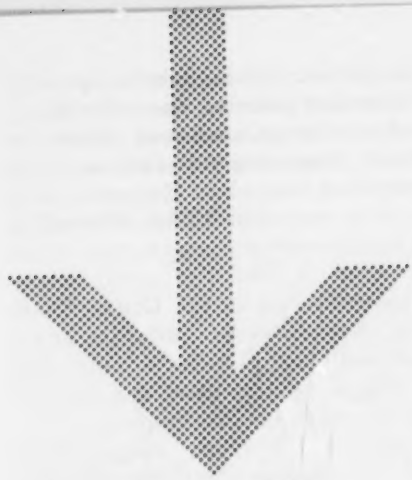

rubella

Rubella, commonly known as German measles, and occasionally also referred to as the "3-day measles," is an infectious disease caused by a virus. Because it is usually a very mild disease and complications are not common, rubella received little attention until 1941, when it became implicated as a cause of congenital malformations in infants whose mothers had the disease in pregnancy.

Following an epidemic of rubella in Australia, Dr. N. M. Gregg, an ophthalmologist, observed a high incidence of cataracts and other anomalies in infants born to mothers who had the disease early in pregnancy. Since this important observation, studies have firmly established the harmful effect of rubella on fetuses and infants. Thus a disease previously considered innocuous is now recognized as a grave threat to the babies of pregnant women who become infected.

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In the United States, rubella attracted special attention following the 1964–65 epidemic when a large number of women infected during pregnancy gave birth to infants with congenital anomalies. Epidemic peaks used to occur every 6 to 9 years. Prevention became feasible with the introduction of live rubella vaccine in 1969, and no major epidemics have occurred in the United States since that time. However, outbreaks of rubella have continued to occur in junior high schools, colleges, military bases, and places of employment—most notably hospitals.

The national Childhood Immunization Initiative, an ongoing effort that began in 1977, includes rubella among the diseases that are being targeted for eradication. The rubella vaccination program was first directed at young children, and the incidence rate for those 14 years of age and under has declined progressively. In the first 3 years of the initiative, the total number of rubella cases decreased by about 40 percent.

Before the vaccine became available, it was estimated that 75 to 90 percent of the people in the U.S. had had the infection by early adulthood, leaving 10 to 25 percent of the population susceptible. The picture had changed somewhat by the 1980s. About 70 percent of the cases now occur in adolescents and adults, with half of these in 15- to 19-year-olds. Thus rubella can no longer be considered primarily a childhood illness.

Incubation period

After a person is exposed to the disease, it generally takes from 2 to 3 weeks for symptoms to develop. This silent interval after exposure is known as the incubation period. A person can spread rubella for about 2 weeks, beginning a week before the onset of the rash. The difficulty of controlling the spread of such a disease is readily apparent, since exposure of susceptible people often

takes place during the incubation period without anyone's knowledge. A single attack of rubella provides long-lasting protection and a second infection is rare.

Signs and symptoms

Typically, rubella has a relatively mild course. In children, a rash may be the first sign of the illness noticed by parents. The rash starts on the face and spreads rapidly down the body and limbs. It usually lasts about 3 days, hence the name "3-day measles." It may disappear before the third day, and occasionally rubella occurs without any rash at all.

The rash, which varies in appearance in different patients, may resemble those caused by measles, scarlet fever, roseola, other viral diseases such as echovirus and Coxsackie virus infections, or rash caused by allergy. Low-grade fever is usually present with the rash. Swelling of the lymph glands behind the ears, in the neck, and at the lower part of the back of the head generally precedes the onset of the rash by a few days. At the beginning, these glands are painful when touched, but the tenderness usually subsides in a day or two, while the swelling persists a little longer. Other symptoms such as general malaise or discomfort, headache, loss of appetite, sore throat, and inflammation of the eyes are more common in adolescents and adults than in children.

Complications in rubella, though less common than in measles, were reported with increased frequency in the 1964–65 epidemic. Arthritis, encephalitis, and a bleeding tendency associated with low blood platelets (a blood element essential in blood clotting) have all been described. Transient arthritic symptoms are so common in adults, particularly women, that they have been considered by some to be an integral component of the disease.

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Diagnosis

The diagnosis of rubella on the basis of signs and symptoms alone has many pitfalls. As mentioned earlier, the rubella rash is often confused with rashes seen in other infectious diseases; or there may be no rash at all. Swollen, tender glands in the locations described are highly suggestive of rubella, yet taken alone they cannot be used to diagnose rubella with certainty. Furthermore, so-called "subclinical infection" occurs frequently with minimal or no apparent symptoms. In the last epidemic many affected infants were born to mothers totally unaware that they had had rubella during pregnancy.

A positive diagnosis of rubella must therefore depend either on isolation of the rubella virus from the throat or other body tissues of the patient, or on blood tests. While isolation of the virus probably indicates a relatively recent infection, a single positive blood test means only that the person has been infected with the rubella virus at some time. To determine whether the infection is recent or not, two blood tests several weeks apart are needed. Usually, one blood specimen is taken as soon as a person is exposed to rubella or, if exposure is not suspected, as soon as symptoms suggestive of rubella appear. A second specimen is taken 2 to 4 weeks later. A significant difference in the results of the two blood tests indicates that the infection is recent.

Until the late 1960s, it took 2 weeks to obtain the results of a blood test. Current techniques make it possible to obtain the results in several hours. The procedure, known as the hemagglutination inhibition (HI) test, can confirm rubella infection in the absence of clinical symptoms and detect immunity years after infection. In most States the test is available from the State health department laboratory. Because of the variation among reagents and technical procedures, results of the HI and other blood tests should be accepted only from

laboratories of recognized competence that perform these tests regularly. To minimize variations and to improve reliability of the test, the Center for Disease Control of the Public Health Service has developed a Standard Rubella HI Antibody Test protocol to guide laboratories performing this test.

Congenital rubella

The importance of rubella lies in its damaging effect on the fetus when a pregnant woman contracts the disease early in pregnancy. The first 3 months of pregnancy is the most dangerous period, but there is evidence that the fetus may also be affected when rubella occurs later. In the last epidemic, some infants born to mothers who had rubella in the second trimester also had hearing defects, delayed language development, mental retardation, or poor physical development.

The exact incidence of affected infants among all infants born after rubella-complicated pregnancies is not known, though it is generally agreed that the earlier the infection, the higher the incidence. It has been estimated that the risk of serious malformation following maternal rubella in the first 8 weeks of pregnancy probably exceeds 50 percent, and these infants are more likely to have multiple anomalies. Risk of serious malformation appears to decrease progressively thereafter, with 20 percent a conservative estimate for the 9th through the 16th weeks.

Affected babies may appear normal at birth and subsequently develop a wide variety of defects. The term "rubella syndrome" refers to the various congenital abnormalities that may be present, either singly or in combination, in infants born of a pregnancy complicated by rubella. Until the 1964–65 epidemic, four main categories of permanent defects were generally included in the rubella syndrome:

1. Hearing loss in one or both ears of varying degree. Often this condition is not detected at birth and sometimes not until a child reaches school age.

2. Eye defects—cataracts, glaucoma, unusually small eyeball, lesions of the retina, and clouding of the cornea not associated with glaucoma.

3. Cardiovascular defects, which also may not be apparent at birth. Patent ductus arteriosus, usually with pulmonary artery stenosis, is by far the most common.

4. Abnormalities of the central nervous system, the most common manifestations of which are abnormally small head, mental retardation, delayed psychomotor development, cerebral palsy, and behavior disturbances, including infantile autism.

The 1964–65 epidemic was the first to be studied with newly developed techniques for virologic confirmation of rubella infection. Abnormal features not usually included in the rubella syndrome were noted in affected infants, although many of them had in fact been described by Gregg in his original report. These are sometimes referred to as features of the "expanded rubella syndrome" or what is more properly called congenital rubella. In contrast to the defects listed above, the following findings (except for nos. 11 and 12) generally are transient and occur in the newborn period.

1. Small size at birth despite a full-term pregnancy. Many of these infants weigh less than 5 pounds at birth. Many have feeding problems and gain weight very slowly. Diarrhea also occurs with some frequency in these infants.

2. Bleeding tendency associated with low blood platelets, known as thrombocytopenic purpura. This is generally manifested in these infants as reddish or purplish spots scattered over the entire body, particularly over the face. Some infants on blood test are found to have abnormally low blood platelets but

present no external evidence of a bleeding tendency.

3. Enlarged liver and spleen.

4. Hepatitis, or inflammation of the liver, usually manifested by jaundice.

5. Swollen lymph nodes. A single node or many in different parts of the body may be involved.

6. Lesions that involve bones of the arms, legs, and skull, detectable only by X-ray.

7. Anemia and occasionally low white blood cell count.

8. Pneumonia.

9. Encephalitis and meningitis, usually indicated by a full or enlarged fontanel, abnormal spinal fluid, irritability, convulsions and other symptoms.

10. Injury of the heart muscles evidenced by symptoms of heart failure and abnormal electrocardiographic tracings.

11. Abnormal fingerprints, palmar creases, and other skin patterns.

12. Other congenital malformations and lesions.

A relatively high mortality rate was reported among affected infants born following the 1964–65 epidemic. Some died shortly after birth, others within the first few weeks or months of life. Studies made during this epidemic confirmed that infants with congenital rubella are infected with the virus in utero. Many are not only infectious at birth, but continue to suffer further damage from the virus after birth.

This is exemplified by the development of eye lesions in some infants after they are born. Rubella virus has been detected in these infants in the newborn period and for several months thereafter and, very rarely, up to 2 years. The virus has also been isolated from apparently normal newborn infants of infected mothers, suggesting that some infected fetuses may escape damage. The most frequent site from which the virus has been recovered is the throat. Other sources re-

ported include urine, feces, spinal fluid, blood, and eyes. Examination of aborted fetuses and infants who have died revealed that the rubella virus can be recovered from almost all organs of the body, including the brain, heart, eyes, lungs, liver, spleen, kidneys, intestines, lymph nodes, skin and bones.

It is thus evident that infants with congenital rubella are capable of spreading the infection and can do so as long as they excrete the rubella virus. They are contagious to persons who come in close contact with them, such as doctors and nurses, if these persons are susceptible.

Care of infected infants

Infants born after a pregnancy complicated by rubella should be carefully examined at birth for possible congenital malformations. Since some of these infants are capable of spreading the infection, isolation has been recommended. (Women working in nurseries or other places where they may come in contact with newborns who are infectious should be considered as potential vaccinees, as described under "Who Should Be Vaccinated.") Regular followup examinations are indispensable even in infants apparently normal at birth, because certain defects like partial hearing loss and mental retardation may not become evident until later. For many of the congenital malformations, such as cataracts, glaucoma, and congenital heart defects, surgery is now possible. Early diagnosis, treatment, and followup care, including special educational services, will improve the outlook for many children born with congenital rubella.

Live rubella vaccine

In 1966, scientists developed a live rubella vaccine, and in 1969 FDA licensed rubella vaccines for general use in the United States.

Clinical experience involving large numbers of vaccinees has fully documented that these vaccines are well tolerated, are highly effective in inducing immunity, and are not contagious.

Who should be vaccinated

Since the live rubella virus vaccine was licensed, the Public Health Service Advisory Committee on Immunization Practices (ACIP) has periodically evaluated available information on rubella and rubella vaccines, and issued recommendations for the use of the vaccine. In its November 1978 statement, the advisory committee recommended rubella vaccine for all children, many adolescents, and some adults, particularly females, unless contraindicated. Vaccination protects children against rubella and prevents their subsequently spreading it. Vaccinating susceptible postpubertal females confers individual protection against rubella-induced fetal injury. Vaccinating adolescents or adult males and females in population groups such as those in colleges, places of employment, and military bases, protects them against rubella and reduces the chance of outbreaks in partially immune groups.

The vaccine is recommended for all children 12 months of age or older. It should not be administered to younger infants because persisting maternal antibodies may interfere with its effectiveness. When the rubella vaccine is part of a combination vaccine that includes the measles antigen, it should be administered to children about 15 months of age or older to achieve maximum rate of protection. Children who have not received rubella vaccine at the optimum age should be vaccinated promptly when the situation is discovered. Because a history of rubella is not a reliable indicator of immunity, all children for whom vaccine is not contraindicated should be vaccinated.

In an August 8, 1980, statement, the committee further pointed out that official health agencies should take steps, including development and enforcement of immunization requirements, to assure that all students in schools and children in day care settings are protected against rubella, unless contraindicated.

The 1978 ACIP statement called for increased emphasis on vaccinating unimmunized prepubertal girls and susceptible adolescent and adult females in the childbearing age group. Because of the theoretical risk to the fetus, females of childbearing age should receive vaccine only if they are not pregnant and understand that they should not become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against rubella, asking females if they are pregnant, excluding those who are, and explaining the theoretical risks to the others are reasonable precautions in a rubella immunization program. When practical, serologic testing of potential vaccinees in the childbearing age group may be undertaken to show susceptibility to rubella.

Educational and other institutions such as high schools, colleges, universities, military bases, and hospitals should seek proof of rubella immunity (a positive serologic test or documentation of previous rubella vaccination) from all female students and employees in the childbearing age. Nonpregnant females who lack proof of immunity should be vaccinated unless contraindications exist.

In discussing the immunization of adolescents and adults against measles and rubella, the 1980 ACIP statement cited current patterns of measles and rubella occurrence, which indicate that outbreaks of these diseases continue to be reported in adolescent and young-adult population groups. Increased attention to school immunization requirements should reduce the incidence in

those of school age. Further control of these diseases will require increased emphasis on vaccinating susceptible individuals who have left high school. The military services have instituted routine measles and rubella immunization of susceptible recruits. Officials of colleges and other settings where young adults congregate should strongly consider immunization requirements for entry. Health care providers should carefully review immunization status of young adults and provide vaccination to those who are not immune and who do not have contraindications.

When there are reliable laboratory services available, routine premarital serology for rubella immunity would enhance efforts to identify susceptible females before pregnancy. Prenatal or antepartum screening for rubella susceptibility should be undertaken and vaccine administered in the immediate postpartum period *prior* to discharge. Previous administration of anti-Rho (D) immune globulin (human) or blood products is not a contraindication to vaccination; however, 6- to 8-week postvaccination serologic testing should be done on those who have received the globulin or blood products to ascertain that seroconversion has occurred. Obtaining laboratory evidence of seroconversion in other vaccinees is not necessary.

In order to protect susceptible female patients and female employees from rubella, all persons working in hospitals and clinics should be immune to the disease so they do not contract rubella from infected patients or transmit rubella to pregnant patients.

There is no evidence that live rubella virus vaccine given after exposure will prevent illness or that vaccinating an individual incubating rubeila is harmful. Since a single exposure may not result in infection and post-exposure vaccination would protect an individual in the event of future exposure, vaccination is recommended unless otherwise contraindicated.

Side effects and adverse reactions

In general, the vaccine has been well tolerated. However, side effects such as rash and lymphadenopathy occasionally occur in children. Joint pain, usually of the small peripheral joints, has been noted in up to 40 percent of vaccinees in large-scale field trials, although frank arthritis is reported in fewer than 1 percent. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in children. When joint symptoms or non-joint-associated pain and paresthesia do occur, they generally begin 2 to 10 weeks after immunization, persist for 1 to 3 days, and rarely recur. The persistent arthritic symptoms that have occasionally been described probably represent coincidental disease rather than vaccine complication. Transient peripheral neuritic complaints such as paresthesia and pain in the hands and feet are uncommon.

Some vaccinees intermittently shed small amounts of virus from the pharynx 7 to 28 days after vaccination. However, studies of more than 1,200 susceptible household contacts have yielded no evidence that vaccine virus has been transmitted. These data strongly suggest that vaccinating susceptible children whose mothers or other household contacts are pregnant does not present a risk.

Although vaccine is safe and effective for all ages over 12 months, its safety for the developing fetus is not fully known. Thus, rubella vaccine is NOT suitable for pregnant women because of the theoretical risk of fetal abnormality caused by the vaccine virus, which does cross the placenta.

Precautions and contraindications

Pregnant women should not be given rubella vaccine. If a pregnant woman is inadvertently vaccinated or if she becomes

pregnant within 3 months of vaccination, she should be counseled on the theoretical risks to the fetus.

Persons with febrile illness should not be vaccinated until they have recovered. Minor illnesses such as upper respiratory infections, however, do not preclude vaccination

Live rubella virus vaccine has not been reported to be associated with allergic reactions and can be given to all who need it, including persons with allergies to eggs, ducks, and feathers. Some vaccines do contain trace amounts of antibiotics, however, to which patients may be allergic. Those administering vaccines should review the label information carefully before deciding whether patients with known allergies to such antibiotics can be vaccinated safely.

Replication of the rubella vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, or generalized malignancy or with therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. Patients with such conditions should not be given live rubella virus vaccine.

Immune serum globulin

Immune serum globulin (ISG) given after exposure to rubella will not prevent infection or viremia, but it may modify or suppress symptoms.

The routine use of ISG for postexposure prophylaxis of rubella in early pregnancy is not recommended. (Infants with congenital rubella have been born to women who were given ISG shortly after exposure.) The only time that ISG might be used is when rubella occurs in a pregnant woman who would not consider termination of pregnancy under any circumstances. Serologic testing for rubella immunity is useful if an exposure in early pregnancy is suspected.

Prevention through vaccination and education

Since the development and widespread use of the rubella vaccine, there has been a 70 percent decline in the number of cases of rubella in the U.S. In the light of these encouraging results, the Nation can look forward to the future when rubella will no longer be a cause of miscarriage, stillbirth, and congenital malformation.

To achieve this, however, major public health efforts will have to be continued throughout the country by local, State, and Federal health agencies working with private practitioners, clinics, health centers, voluntary agencies, parents, and communities. The focus must be—

1. To increase public awareness of the need for immunization.
2. To maintain immunization at an acceptable level.

The program must include public education as well as vaccination. During the 1964–65 epidemic, for example, many women—particularly those in low-income groups—did not know of the causal relationship between the disease and congenital malformations. Much of the general public is still not aware of the significance of rubella.

The problem of congenital rubella has not disappeared, although no major epidemic has occurred in the U.S. since the vaccine was introduced. Unprotected women infected during pregnancy have continued to give birth to babies with congenital anomalies caused by rubella. Health workers as well as the public must therefore understand the importance of continuous education and vaccination programs in preventing future epidemics and their tragic consequences.

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